REMARKS

In the instant amendment, claims 14 and 17 have been amended. New claims 20 and 21 have been added. After entry of the instant amendment, claims 14-21 will be pending and under consideration.

I. AMENDMENT TO THE CLAIMS

Claims 14 and 17 have each been amended to recite, in relevant part, that Z_2 is -C(O)R, -C(O)OR, -C(O)NHR, or -C(O)NRR, to conform with proper expression where each of the specified constituents are alternatives for Z_2.

New claims 20 and 21 re-present claims 14 and 17 respectively, except that new claims 20 and 21 recite, in relevant part, that Z_2 is -C(O)OH, *inter alia*. New claims 20 and 21 are supported by the specification, for example, at page 14, line 14-15, and page 15, lines 7-29.

As the amendments to the claims are supported by the specification and claims as filed, entry thereof is kindly requested.

II. REJECTION OF CLAIMS 14-19 UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 14-19 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly requiring undue experimentation to practice across their scope. In short, the Patent Office contends that the genus of compounds encompassed in the claims is very large with many of the peptides therein having an unpredictable activity with regard to the transferrin receptor thus requiring undue experimentation for one of skill to practice claims 14-19. Applicants respectfully traverse.

From the outset, Applicants note that "[a] single working example in the specification for a claimed invention is enough to preclude a rejection which states that nothing is enabled since at least that embodiment would be enabled." MPEP § 2164.02. Also, Applicants believe that claims 16 and 19 should not be included in the rejection since the Patent Office's remarks for lack of enablement as requiring undue experimentation, which are discussed below, are clearly directed to claims 14, 15, 17 and 18. Claims 16 and 19 recite the particular amino acids, *i.e.*, structure, that must be present for each position in the peptides recited in each method of claims 16 and 19. Since claims 16 and 19 should not have been included in the rejection, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, for those claims be withdrawn.

A. The Legal Standard

The legal standard for enablement under 35 U.S.C. § 112, first paragraph, requires that the specification teach those in the art to make and use the invention without undue experimentation. *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). The Federal Circuit elaborated that whether undue experimentation is needed is not a single, simple factual determination, but a conclusion reached by weighing many factual considerations, and listed eight exemplary factors (the "*Wands* factors"). *Id.* The Patent Office applies the *Wands* factors and concludes that undue experimentation is required to practice each of claims 14-19. Applicants respectfully submit that an analysis of the *Wands* factors requires the opposite conclusion.

B. Application of the *Wands* Factors

1. The Breadth of The Claims and The Relative Skill of Those in the Art

Claim 14 recites a seventeen residue compound wherein the amino acid residues are defined based upon their classification as aromatic, aliphatic, acidic, etc., other than X_{13} which is isoleucine. Thus, there are definitions on what sort of residue may exist at each of the seventeen positions. Applicants have further demonstrated that one embodiment, SEQ ID NO:1 is active in reducing cell-associated binding of transferrin. Since the skill in the Art is high, as acknowledged by the Patent Office, Applicants submit that it is rather straightforward for one of skill to make a conservative substitution in the SEQ ID NO:1 embodiment, guided by Table I of the specification, for instance, and test the substituted peptide's activity on TfR, guided by the specification at page 26, for instance, thereby making a combination of the recited compound of the claims that is active as defined on page 16, lines 19-23 of the specification. Thus, the claims are not too broad in view of the relatively high skill in the Art.

2. The Predictability Or Unpredictability of the Art

The Patent Office asserts that computer models are not absolute prediction tools for the activity of a compound, such as the proverbial magic bullet, or the folding of a protein, citing Ngo *et al.* in *The Protein Folding Problem and Tertiary Structure Prediction* and an article in *Science* **256**: 441 (1992). The specification on pages 2-3 describes how the alpha-1 region of the HFE protein was the "model" for developing the compounds recited in the

instant claims. The results on page 27 evidence that an embodiment of the compounds recited in claims 14 or 17, for example, does in fact have the useful activity of reducing cell-associated binding of transferrin. Fortunately, no computer modeling is necessary for one of skill to make a compound for use in the method of claim 14 or of claim 17. As stated above, Applicants submit that it is straightforward for one of skill in the art to construct a compound having the residues meeting the characteristic identified for each X position in formula (I) using, for example, Table I on page 13 of the specification as a guide, and then test its activity on the function of TfR, as described on page 26, for example. Therefore, Applicants submit that the art is more predictable than the Patent Office would attribute to it.

3. The Amount of Direction or Guidance

The Patent Office states that the amount of guidance given by the specification is in the form of a single sequence, SEQ ID NO. 1, to demonstrate the desired activity. However, the specification is replete with guidance on synthesizing, purifying, testing for activity, formulating and administering compounds such as recited in claims 14-19. Thus, rather than focus on whether one of skill in the art can practice the invention using the direction supplied by the specification, the Patent Office appears to dispute that peptides, other than SEQ ID NO. 1, encompassed in the recited compound of claim 14, for example, *would be active* in reducing cell-associated binding of transferrin. This concern is appropriately addressed below. Applicants submit that the amount of direction or guidance in order for one of skill to practice the methods of claims 14-19 weighs in Applicants' favor.

4. The Presence or Absence of Working Examples and The Quantity of Experimentation Necessary

The Patent Office alleges that specification's lack of working examples, other than that of SEQ ID NO:1, indicates that "undue painstaking experimentation study" is required to determine if the recited compounds would be active in reducing cell-associated binding of transferrin. Applicants respectfully disagree. The specification clearly demonstrates that SEQ ID NO:1, one combination of the compounds recited in claims 14-19, has activity in reducing cell-associated binding of transferrin. Hence, there is no need to "develop a drug from scratch" as discussed in the cited Science article, since the compounds encompassed in the claims are merely conservative substitutions at one or more of sixteen positions out of seventeen. The only experimentation needed is to test for activity of a particular compound in the cell-based assay described in the specification, which Applicants submit is not unlike

routine screening of hybridomas allowed in *In re Wands*. That some of the combinations of the compound recited in claim 14 or 17 may be inoperative is no barrier to patentability under 35 U.S.C. § 112, first paragraph. *See Atlas Powder Co. v. E.I. Du Pont De Nemours & Co.*, 224 U.S.P.Q. 409, 414 (Fed. Cir. 1984) ("'It is not a function of claims to specifically exclude . . . possible inoperative substances . . . .'"). Since the sorts of substitutions to the recited compound of claim 14 are the conservative substitutions defined in the claim itself, and since performing the cell-based activity assay for a combination of the recited compound is not itself unduly difficult for one of skill in the art, Applicants submit that quantity of experimentation to test for activity of a compound does not amount to undue experimentation.

4. The Nature of the Invention and The State of the Prior Art

Regarding the nature of the invention, the Patent Office states that claims are drawn to a "method of inhibiting TfR binding to transferrin or method of treating iron overload disease using polypeptide." With regard to the state of the prior art, the Patent Office states that the art does not recognize the ability of peptides, similar to those claimed, that inhibit TfR binding to transferrin or method of treating iron overload disease. With due respect, it appears to Applicants that these two *Wands* factors are neutral as characterized by the Patent Office, and do not support a conclusion of "undue experimentation."

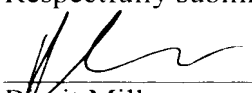
Applicants respectfully submit that the *Wands* factors weigh against a finding of undue experimentation for claims 14-19. Accordingly, Applicants respectfully request that this rejection of claims 14-19 under 35 U.S.C. § 112, first paragraph, be withdrawn.

CONCLUSION

In light of the above amendments and remarks, the Applicant respectfully requests that the Examiner reconsider this application with a view towards allowance. The Examiner is invited to call the undersigned attorney if a telephone call could help resolve any remaining items.

Respectfully submitted,

Date: August 26, 2003



43,341

Birgit Millauer (Reg. No.)
For: Brian M. Poissant, Reg. No. 28,462
PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090

CAI 3500201